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Childhood dietary exposure of aflatoxins and fumonisins in Tanzania: A review

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Abstract: Aflatoxins (AFs) and Fumonisins (FBs) are common contaminants of maize, from secondary metabolites of fungi. Presence of AFs and FBs in maize-based complimentary food is evident in various studies conducted in Tanzania and elsewhere. Consequently, Infant and Young children (IYC) aged between 6 and 24 months in Tanzania who consume monotonous maize-based foods are at a high risk of exposure to these toxins. The AF or FB exposures have been linked to low awareness and inadequate knowledge or limited skills of IYC feeding practices among mothers and caregivers. This review reveals that more researches are needed to identify appropriate feeding practices in Tanzania to improve child growth. Meanwhile, stakeholders should direct efforts on education to subsistence farmers including mothers and caregivers on interventions to minimize mycotoxin contamination of cereal and nut-based complementary foods in the country.

Subjects: Biochemistry; Biology; Food Additives & Ingredients; Food Chemistry; Food Laws & Regulations; Health and Safety; Environmental Health & Safety; Risk Assessment; Adult Education and Lifelong Learning; Health & Society

Keywords: Mycotoxins; exposure; children; feeding practices; aflatoxins; fumonisins Tanzania

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PUBLIC INTEREST STATEMENT

Complementary foods (CFs) given to Infants and Young Children (IYC) between 6 and 24 months to complement breast milk assure their optimal growth and development. CFs in Tanzania are mainly based on cereals, in particularly maize gruel, that are susceptible to aflatoxins (AFs) and fumonisins (FBs) contamination. This paper reviewed AFs and FBs contamination in maize-based CFs as well as exposure and effects on child growth. It also reviewed available literature on awareness of AFs and FBs among mothers and caregivers. Awareness of good agricultural practices, AFs and FBs management, and appropriate complementary feeding interventions can lessen the burden of aflatoxins and fumonisins exposure in communities relying on aflatoxin and fumonisin prone foods.

1. Introduction

The major foods in Tanzania (and elsewhere) are prone to infection by unpredictable and unavoidable fungi such as *Aspergillus, Penicillium, Claviceps* and *Fusarium* spp (Adeyeye, 2016; Leggieri et al., 2019; Kagot et al., 2019; Kimanya et al., 2014). The fungi can infiltrate deep into the matrices of cereal crops or other produces and produce invisible and toxic secondary metabolites (mycotoxins), at different stages along the food chain. More than 60–80% of the world cereal grains are contaminated with mycotoxins (Eskola et al., 2020).

Mycotoxins occurrence has shown regional disparity determined mostly by weather and climate differences. Mycotoxins are currently reported to be less prevalent in foods consumed in the developed compared to developing countries. In a study of 27 samples of dried pasta characterized by size, packaging, and marketing intended for young children consumption in Italy, no samples were found to be contaminated by aflatoxin B1 (AFB1) (Raiola et al., 2012). The prevailing tropical and subtropical climate of the developing countries in Africa and Asia attracts fungal growth and mycotoxin production in food (Gruber-Dorninger et al., 2019; James & Zinkankuba, 2018; Lee & Ryu, 2017; Medina et al., 2014). In their study, Lee and Ryu (2017) reported the occurrence of AFs with an incidence rate of 50% in raw cereal grains in Africa (Lee & Ryu, 2017). Their findings corroborate earlier findings by Darwish et al. (2014) on the level of aflatoxins (AFs) in maize in Africa. In Asia, incidence as high as 63% for AFs in corn was also reported (Lee & Ryu, 2017).

In one study of fumonisins (FBs) in Tanzanian maize, the toxins were determined in 52% of samples at levels up to11,048 µg/kg and in 15%, levels exceeded 1,000 µg/kg (Kimanya et al., 2008). In this study, AFs were detected in 18% of the samples at levels up to 158 µg/kg. Twelve percent of the samples exceeded the Tanzanian limit (10 µg/kg) for total AF. AFs co-occurred with FBs in 10% of the samples. Additionally, in a study of maize sampled in three districts of Tanzania as reported in 2015, noticeable high occurrence (50%) of AFB1 and fumonisin B1 (FB1) (73%) were detected (Kamala et al., 2015). In 2017, another study reported contamination levels from maize-based complementary food intended for infant and young children (IYC) in Tanzania, ranging from 0.44 to 1081 (µg/kg) for AFs and 18–56,400 (µg/kg) for FBs (Kamala et al. (2017). The hot temperatures in combination with high humidity in sub Saharan Africa (SSA) and Asian countries favor high prevalence of AF and FB contamination in maize and maize-based products (Bankole et al., 2006; Benkerroum, 2020; Gruber-Dorninger et al., 2019; Kamle et al., 2019; Lukwago et al., 2019). However, it should be noted that climate change is threatening to alter the mycotoxin prevalence level and contamination rate in foods due to inconsistency in rainfall patterns and rises in temperature and carbon dioxide levels in various parts of the world (Ramirez-cabral et al., 2017; Wheeler & von Braun, 2013).

Generally, optimum conditions for AF production is a temperature of 33°C and water activity of 0.99 while that for fungal growth is 35°C and water activity of 0.95 (Milani, 2013). Tanzania lies between latitudes 1°S and 12°S and has an annual average temperatures range from 25 to 32°C (Luhunga et al., 2018) with maximum daily temperature range of 35 – 38.4°C in some parts (Kiunsi, 2013; Tanzania Meteorological Authority [TMA], 2019).This provides a conducive climate for maize production as well as AF production and growth. Tanzania has two long and short rainfall seasons depending on locations (Luhunga et al., 2014; United Republic of Tanzania [URT], 2010; Verheye, 2010). Areas with the short rain seasons are less productive and thus most parts of the country rely on the long rains for food production. As a result, maize is stored for long durations to cater for food during the off season. Extended period of storage makes maize vulnerable to mycotoxins contamination (Bennett & Klich, 2003; Sasamalo et al., 2018).

Maize is a natural choice of a staple food for majority of Tanzania and is a key crop to enhance food production, income, poverty alleviation, and food security in the country (Food and

Agriculture Organization Corporate Statistical Database [FAOSTAT], 2019; Homann-Kee Tui et al., 2013; Pauw & Thurlow, 2011). Almost 75% home-grown maize in Tanzania is used for human consumption at an average rate of 349 g/person/day.

Additionally, mothers in Tanzania use maize as a sole or major component in complementary food (G Chen et al., 2018; C Chen et al., 2018; Kamala et al., 2018; Kulwa et al., 2015; Makori et al., 2018; Shirima et al., 2015).

Consumption of mycotoxin-contaminated food may lead to acute and chronic toxin exposures (Tola & Kebede, 2016; Wild & Gong, 2010) that are detrimental to the children's health (Raiola et al., 2015). Reports of AF exposure and multiple exposures in maize-based complementary food are available for Tanzania. In a study from three agro-ecological zones of Tanzania by Kamala et al. (2017), AF probabilistic exposures among infants ranged from 700 to 716 ng/kg/bw/day in Eastern Lowland, 13.4–14.3 ng/kg/bw/day in Northern Highland and 9.2–9.7 ng/kg/bw/day in Southwestern Highland.

Likewise, in 2013, another study in three regions (Iringa, Tabora, and Kilimanjaro) of Tanzania, looked at the AF exposures in infants and found that of146 children, 84% were positive for AF—Albumin. In Iringa the range of AF-Albumin levels was 13.5–29.2 pg/mg, in Tabora, 28.7–65.0 pg/mg and in Kilimanjaro, 2.8-4-7 pg/mg (Shirima et al., 2013).

Exposure to AFs or FBs is associated with myriad health consequences including IYC growth impairment (C Chen et al., 2018; Kimanya et al., 2010, 2014; Shirima et al., 2015). The main routes of AF and FB exposures are complementary foods (Kamala et al., 2015; Kimanya et al., 2008, 2014; Makori et al., 2018; Shirima et al., 2015) and consumption of raw or heated cow milk (Mohammed et al., 2016; Urio et al., 2006). Reports of AF exposure through utero and breast milk in Tanzania are found in the works of Passarelli et al. (2019) and Magoha et al. (2014a), respectively.

This review covers literature on AFs and FBs exposure in maize-based complementary foods and the evidence of association between the exposure and poor growth status of IYC in Tanzania. It also discusses gaps in awareness and knowledge of child feeding practices appropriate to prevent dietary exposure of AF and FB in Tanzanian IYC.

2. Nature and toxicity of aflatoxins

Historically, AFs were first discovered in the 1960s in the UK following an outbreak of "turkey X" disease (Blount, 1961). These toxins are mostly produced by *Aspergillus flavus and Aspergillus parasiticus (*Bryden, 2012).

A. flavus produces AFB1 and aflatoxin B2 (AFB2) while *A. parasiticus* produces both B and G forms (aflatoxin G1 -AFG1 and aflatoxin G2—AFG2) of AFs. The International Agency for Research on Cancer (IARC) classifies naturally occurring AFs as class 1 carcinogens, meaning that they have been confirmed to cause liver cancer in most animal species studied and in humans (International Agency for Research on Cancer [IARC], 1993). Although, hepatocellular carcinoma (HCC) is mainly caused by Hepatitis B Virus (HBV) (Wild & Hall 2000), there is increasing incidence of HCC in areas with individuals chronically infected with HBV and exposed to AFs (IARC, 2002), suggesting a synergistic effect in liver damage.

When livestock ingest AFB1-contaminated feed, they excrete the principal 4-hydroxylated form aflatoxin M1 (AFM1) in milk and urine (International Agency for Research on Cancer/World Health Organization [IARC/WHO], 2012). Likewise when lactating mothers consume AFB1-contaminated food they excrete AFM1 in human milk (European Food safety Authority [EFSA], 2020). AFM1 has been classified by IARC as a possible human carcinogen in class 2B (IARC/WHO, 2012).

3. Aflatoxin contamination and exposure in Tanzania

Kimanya et al. (2008) detected AFs in 18% of 129 maize samples from four regions of Tabora, Ruvuma, Kilimanjaro, and Iringa in Tanzania, at levels of up to 158 µg/kg. Twelve percent of the samples exceeded the Tanzanian limit (10 µg/kg) for total AFs. In another study in Dodoma region of Tanzania, Makori et al. (2018) reported AFB1 contamination in 42.5% of complementary flours. The levels ranged from 0.25 to 2,128.1 µg/kg. Total AFs (AFB1 + AFB2 + AFG1 + AFG2) ranged from 0.40 to 2,129 µg/kg and in 30.6% of samples, levels were above the limit of 10 µg/kg.

For three regions of Manyara, Morogoro, and Mbeya, Kamala et al. (2015) reported that 50% of all maize-based food intended for direct human consumption were contaminated with at least one of the tested AFs (AFB1, AFB2,AFG1, or AFG2). In the contaminated samples, 28% and 8%, respectively, were above maximum limit of 5 and 10 µg per kg for AFB1 and AF total.

In another study in Manyara region, AFs were detected in 32% of maize samples (mean 3.4 ± 0.3 µg/kg; range 2.1–16.2 µg/kg; Nyangi et al., 2016), whilst in a survey of AFM1 exposures in IYC in Kongwa and Kiteto districts around central Tanzania, Urinary exposure was detected with a mean and maximum levels of 57.1 pg/ml and 614 pg/ml, respectively (Anitha et al., 2020).

Aflatoxin B1-lysine (AFB1-lys) biomarker concentrations were also analyzed for children in Haydom Tanzania (C Chen et al., 2018). The report revealed that 72% of the children had detectable AFB1-lysine, with a mean level of 5.1 (95% CI: 3.5, 6.6) pg/mg albumin.

A study of 148 young children aged 12 to 22 months by Shirima et al. (2013) in three geographically distant villages of Iringa, Tabora, and Kilimanjaro regions in Tanzania, revealed the chronic exposure of young children to AFs through contaminated maize diet. AF exposure biomaker was detectable in 84% of children and was highest in children who were fully weaned and consuming maize-based foods. The various studies so far conducted show that AFB1 is the most prevalent and toxic of the other forms. However, no study has investigated the linkage between AFs and genotoxicity or immunosuppression in Tanzania.

4. Nature and toxicity of fumonisins

The FBs were first isolated in 1988 by Gelderblom who isolated fumonisins B1 and B2 from Fumonisin moniliforme MRC 826 in rats when investigating the hepatotoxicity and hepatocarcinogenicity of the fungi (Gelderblom et al., 1988). FBs analogs, comprising toxicologically important FB1, FB2, and fumonisin B3 (FB3), are the most abundant naturally occurring forms of FBs in maize and maize-based products (Rheeder et al., 2002).They are produced mainly by the fungi *Fusarium verticillioides* and *Fusarium proliferatum* species that commonly infect maize (corn) and maize-based products worldwide.

FBI usually constitute about 70% of the total FBs content found in naturally contaminated foods and feeds (EFSA, 2005). This form of FBs (FB1) was classified as a group 2B, possible human carcinogen (IARC/WHO, 2012; IARC, 2002). The liver, kidney, and intestine have been reported as the main target organs for FBs toxicity (Bouhet & Oswald, 2007; Voss et al., 2007).

The 74th Joint FAO/WHO Expert Committee on Food Additives (JECFA) committee meeting established a group Provisional Maximum Tolerable Daily Intake (PMTDI) of 2 µg/kg bw for FB1, FB2 and FB3, alone or in combination, on the basis of a lower 95% confidence limit on the benchmark dose for a 10% response (BMDL10) of 0.165 µg/kg bw per day and an uncertainty factor of 100 (Joint FAO/WHO Expert Committee on Food Additives [JECFA], 2017).

5. Fumonisin contamination and exposure in Tanzania

In Tanzania, IYC consuming maize and maize-based complementary foods are reported to be at a high risk of FBs exposure. Kimanya et al. (2010) and Shirima et al. (2013) found that IYC who were consuming maize-based foods were at a high risk of exposure to FBs. Kimanya et al. (2010)

found that FBs exposure in 26 of 215 infants exceeded the PMTDI of 2 μg/kg body weight. The researchers also observed an association between FBs exposure from maize and growth retardation among the infants in Tanzania. Specifically, they observed that at 12 months of age, infants with exposure to FBs above the PMTDI were significantly shorter by 1.3 cm and 328 g lighter when compared to their counterparts.

Shirima et al. (2013) evaluated the status of dietary FBs exposure in young Tanzanian children from Kigwa, Nyabula, and Kikelelwa villages, using a urinary biomarker of exposure. Urinary FB1 was detectable in 96% of children with mean values of 327.2, 211.7, and 82.8 pg/mL in Kigwa, Nyabula, and Kikelelwa, respectively. The researchers observed a clear association between frequencies and quantities of contaminated maize consumed and the quantities of excreted FB1. Similarly, Kimanya et al. (2014) and Kamala et al. (2017) found that IYC in Tanzania are at a high risk of exposure to FBs in maize-based complementary food. As children in Tanzania and Africa – in general – rely mostly on monotonous maize-based diet shifting from maize to other types of complementary diets such as rice and pumpkin is suggested as one of the measures to minimize the risk of exposure to the toxins.

6. Co-exposure of fumonisins with aflatoxins in Tanzania

Co-exposure to FB1 with AFB1 is a concern because of the known genotoxicity effect of AFB1 and the ability of FB1 to induce regenerative proliferation in target tissues (JECFA, 2012). maize-based complementary foods may cause a risk of combined exposures to AF and FB to IYC in Tanzania. Various studies have shown co-occurrence of FB1 and AFB1 in Tanzanian maize (Geary et al., 2016; Kamala et al., 2015; Kimanya et al., 2008, 2014; Nyangi et al., 2016; Shirima et al., 2013, 2015; Suleiman & Rosentrater, 2015). For instance, in Kimanya et al. (2014), AFs and FBs co-occurred in 29% of samples from maize flour intended for complementary food.

Similarly, a longitudinal study of multi-mycotoxin occurrence in maize-based porridges from selected regions of Tanzania by Geary et al. (2016) revealed co-occurrence of mycotoxins in IYC maize-based diet. The study detected and quantified myriad combination of mycotoxins that include AFB1, AFB2, AFG1, AFG2, FB1, and FB2 in 101 samples of maize-based porridges. Result showed that 82% of samples were co-contaminated with more than one group of mycotoxins. Fumonisins (FB1+ FB2) had the highest percentage occurrence in all 101 samples (100%). Other studies of co-occurrence of AF and FB with other mycotoxin in Tanzania were reported by Shirima et al. (2013), Magoha et al. (2014b), Shirima et al. (2015), Kamala et al. (2015), Kamala et al. (2016), and C Chen et al. (2018).

7. Effects of AF and FB exposure on IYC Health in Tanzania

Mycotoxins, in particular of a type AF and FB as detected in contaminated maize and maize-based products in the East African region are evidently a major health concern (Kimanya, 2015). IYC are at a continuous and high health risk (Kimanya et al., 2008, 2009; Modest 2017; Urio et al., 2006) because of their relatively small body weight and underdeveloped immunity.

As previously stated AFs and FBs exposures in Tanzania have been associated to stunting. By the WHO classification, a child with low height for age (height-for-age below −2 SD) is considered to be stunted. Tanzania ranks first in burden of stunting in East Africa (34.4%), followed by Uganda (33.4%) and Kenya (26.0%) (Akombi et al., 2017). This level of stunting is still considered very high, according to the new WHO-UNICEF classification (≥30%) and raises a major concern.

8. Main determinants of AF and FB exposures in Tanzanian Children

The dietary determinants of mycotoxin exposure in children are the type and amount of the food given. Generally, breast milk is safer than normal foods. Thus, introduction of complementary foods earlier than the recommended 6 months of age which is a common practice in Tanzania (Kinabo et al., 2017; Kulwa et al., 2006; Nkala & Msuya, 2011) increases the risk of mycotoxins exposure to infants. The 2015 national health survey, showed that 41% of infants in Tanzania were not exclusively breastfed (Ministry of Health, Community Development, Gender, Elderly and Children (MoHCDGEC) [Tanzania Mainland] et al., 2016).

Mothers in Tanzania use maize as the major ingredient of complementary food (Kimanya et al., 2012; Kinabo et al., 2017; Kulwa et al., 2006, 2015; Makori et al., 2018). Kimanya et al. (2014) estimated that maize flour consumption in complementary foods of Tanzania range from 16 to 254 g/child/day. Given the already described high contamination of AFs and FBs in Tanzanian such a high consumption of maize (16–254 g/child/day) presents a very high risk of exposures of public health concern.

Maternal and caregiver unawareness about the problem of mycotoxin contamination in maize and inadequate knowledge about appropriate complementary feeding are the main reasons for the early introduction of maize-based complementary food in Tanzania. In a study conducted in Dodoma Tanzania, awareness of adequate practices for IYC feeding among parents was found to be 35% (Makori et al., 2018). Generally, extension services on child feeding are inadequate and rare. Mothers and caregivers, especially in rural communities, rely on education from previous generations. A study in Mvomero Morogoro reported that 61% of mothers received child feeding information from their mothers, grandmothers (Mbwana, 2012).This calls for assessment of the awareness and knowledge about mycotoxins exposure and complementary feeding practices in Tanzania to formulate strategies to minimize childhood exposure to mycotoxins in the country.

9. Strategies to mitigate AF and FB exposures in complementary food in Tanzania

Training mothers or child caregivers, who are also farmers in most Tanzanian rural settings, on appropriate pre and post-harvest handling practices, is reported as one of the effective intervention to reduce mycotoxin exposure in maize used for complementary food (Anitha et al., 2020). In their study, Anitha et al. (2020) exclusively focused on training of mothers (farmers) on dietary diversification, food safety and proper hygiene practices. They educated mothers on the consequences of AFs exposure and ways to reduce AFs contamination. The appropriate pre and post-harvest methods taught included mulching, harvesting without damaging pods or cobs, drying on a sheet rather than on soil, drying adequately to reduce moisture, sorting of damaged and rotten grain from the lot to be ground into flour, and using proper storage. After intervention the mean AFM1 level decreased from 57.1 pg/mL to 20.3 pg/mL and 60.3 pg/mL to 53.6 pg/mL in the intervention and control groups, respectively. It's worth noting that after intervention dietary diversity increased from 3 food groups to 5 food groups. Other effective pre-harvest interventions reported in Tanzania are intercropping farming system (Seetha et al., 2017).

In general, recommended post-harvest practices to mitigate AF and FB contamination in maize and maize-based products in Tanzania include (hand) sorting, rapid drying on platforms to avoid direct contact with soil, proper shelling methods, de-hulling of maize prior to milling, sorting to remove bad grain from the lot, use of clean and aerated storage structures, controlling insect damage, good transportation practices, and avoiding long storage periods, 8–10 months, lactic acid fermentation, washing, and winnowing of maize grains (Anitha et al., 2020; Ayalew et al., 2017; Kamala et al., 2018; Nyamete et al., 2016; Seetha et al., 2017; Siwela et al., 2005; Suleiman et al., 2017).

Ayalew et al. (2017), reviewed AF prevention strategies at pre-harvest stage in Africa in general. Their review provided hints to be applied in the context of mycotoxins prevention in maize in Tanzania. The review broadly classified intervention into three parts; enhancement of the host (crop) fungal resistance, the avoidance of fungal contamination, and the reduction of toxigenic fungal population. Farmers were advised to adopt crop rotation, tillage, timely planting of agro-ecologically adapted varieties or disease-resistant varieties, appropriate levels of crop density, irrigation and fertilization management, weed control, effective disease and pest management, including the use of biocontrol agents.

At the regional level, The African Union Commission (AUC) through the Partnership for Aflatoxin Control in Africa (PACA) extended assistance to Tanzania to identify concrete investment options for the country in the area of food safety with focus on AF control (The Partnership for Aflatoxin Control in Africa [PACA], 2016). This assistance came after recognizing that proper implementation of the Tanzania Agriculture and Food Security Investment Plan (TAFSIP) cannot be fully realized without inclusion in it of a comprehensive AF Strategy and Investment Programme. Strategic actions at pre-harvest and post-harvest for mitigation of the AF (as well as FB) in Tanzania were developed and are currently being implemented through a Global Agriculture and Food Security Program (GAFSP) supported project, "Tanzania National Initiative for Aflatoxin Prevention and Control (TANIPAC)". This is a five-year project launched in 2018 to minimize AF occurrence in the food system through an integrated approach in the maize and groundnut value chains with the overall impact of improving food safety and food security, which will ultimately improve the health and nutrition of the communities, improve agricultural productivity, and boost trade.

In view of the above, researchers should consider more interventions that includes education of proper management and handling of maize during pre- and post-harvest periods.

10. Conclusion

We have reviewed the contamination, exposure, and effects of two major mycotoxins (AFs and FBs) in maize and maize-based complementary products in Tanzania. The risk of health effects of AFs and FBs among IYC in Tanzania was assessed to be high. As the country is located along a conducive corridor for maize production by majority of farmers as staple diet, and as they continue to rely on suboptimal complementary feeding on maize-based CF, the risk of AFs or FBs exposure among IYC will consistently remain high. Reports of AF exposure and multiple exposures in maize-based complementary food were obtained for all five geographical distant zones of Tanzania; the Eastern, Western, Northern, Southern zones and Highlands of Tanzania (Kamala et al., 2015; Kimanya et al., 2010, 2008, 2014; Makori et al., 2018; Shirima et al., 2015).

The reports provide the evidence that exposures of AFs and FBs is associated with child stunting in Tanzania and that the exposures are linked to the existing poor feeding practices. Mothers/caregivers in the rural areas (in particular) seem to have little knowledge on proper IYC feeding practices and awareness of mycotoxin contamination in complementary food. Identification of locally achievable best child feeding practices (through research), formulation of appropriate complementary feeding guidelines, and continuous dissemination (through health/agricultural extension services) of the guidelines to mothers and caregivers can have considerable contribution to minimization of AFs and FBs contamination and exposure in maize-based complementary foods in Tanzania. We conclude that in addition to focusing on household dietary diversity and food security interventions, stakeholders should direct efforts on education to subsistence farmers including mothers and caregivers of IYC, on proper pre and post-harvest management and handling of maize-based complementary foods to minimize the impacts of AFs and FBs exposures in Tanzania.

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Competing Interests
The authors declared that they have no competing interest.

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